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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,725	04/23/2001	Hans-Werner Heinrich	101195-44	4120

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EXAMINER	
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ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/786,725	HEINRICH ET AL.	
	Examiner	Art Unit	
	JAMES L. GRUN	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1,3,6,8,9,12-15,17-19 and 24* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,3,8,9,17-19 and 24* is/are rejected.

8)☒ Claim(s) *1,3,6,8,9,12-15,17-19 and 24* is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☒ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Notice to comply…Sequence Disclosures.

DETAILED ACTION

Amendment Entry

The amendment filed 23 November 2011 is acknowledged and has been entered. Claims 1, 3, 6, 8, 9, 12-15, 17-19, and 24 remain in the case.

Sequence Compliance

As set forth in the prior Office action mailed 26 December 2007, this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

All disclosed sequences, e.g. all the sequences disclosed on Substitute Specification pages 4, 5, 7, and 9 and in currently pending claims 1, 6, 15, and 17, are not listed in the computer readable form of the Sequence Listing currently of record in the application as required. The examiner would note that: the sequence disclosed in the specification and claims as SEQ ID NO: 3 is listed in the computer readable form of the Sequence Listing currently of record as both SEQ ID NO: 3 and SEQ ID NO: 4; and, the sequence disclosed in the specification and claims as SEQ ID NO: 4 is not listed in the computer readable form of the Sequence Listing currently of record. A paper copy

of the Sequence listing, and an asserted computer readable form of the Sequence Listing, were indicated by applicant as filed on 27 May 2008. However, only the paper copy of the Sequence Listing filed on that date is of record and thus the reply filed on 27 May 2008 has been found, upon further consideration, as not fully responsive to the prior Office action. Appropriate correction is required.

Applicants are required to provide a substitute copy of the "Sequence Listing" in computer readable form, containing each of the sequences disclosed in the specification and the same in content as the paper copy of the "Sequence Listing", filed 27 May 2008, as required by 37 CFR 1.821(e). If the copy of the sequence listing is filed electronically by EFS it should be filed as the ASCII text document of the Sequence Listing not the PDF document. Applicants must also provide a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 8, 9, 17-19, and 24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 and claims dependent thereupon, "said polyclonal antibodies that react specifically with" iso-enzyme lack antecedent basis because polyclonal antibodies raised against synthetic peptides are previously claimed and, thus, the interrelationships of the components and steps of the method are not clear. It is also noted that the format for the recitation of SEQ ID NO: 1 is internally inconsistent in that a "-" is not present between the Val and Ala residues.

In claim 3, improper Markush language is used to claim the members of the group. The alternatives "selected from...or" or "selected from the group consisting of...and" are acceptable.

In claim 17 and claims dependent thereupon, the interrelationships of the kit components are not clear because it is not clear which of the one or more antibodies are bound to a carrier or if all of the antibodies are bound to a carrier.

In claim 18, the interrelationships of the components are not clear because it is not clear if both antibodies are to be bound to the same carrier and how this relates to a sandwich test kit.

Applicant's arguments filed 23 November 2011 have been fully considered but they are not deemed to be persuasive. Notwithstanding applicant's assertions to the contrary, applicant's amendments have not obviated rejections under this statute for the reasons set forth above.

Claim Objections

Claims 1, 3, 6, 8, 9, 15, 17-19, and 24 are objected to because of the following informalities: the sequence disclosed in the specification and claims as SEQ ID NO: 4 is not listed in the computer readable form of the Sequence Listing currently of record.

Claim 6 is objected to because of the following informalities: the claim would more clearly claim the subject matter which applicant regards as the invention if --kit-- is recited at line 1, --wherein the polyclonal antibodies are purified-- instead of "where the antibodies are" is recited at line 3, and --specifically bind-- instead of "can recognize" is recited at line 9.

Claims 12-15 are objected to because of the following informalities: it is noted that the format for the recitation of each of SEQ ID NOs: 2-5 in these claims are each internally inconsistent in that a "-" is not present between certain pairs of amino acid residues. Appropriate correction is required.

Examiner's Remarks

The following are presented for applicant's consideration upon bringing the application in compliance with the sequence rules. The examiner would suggest cancellation of claims 1, 3, 6, 8, 9, 17-19, and 24 and addition of the following:

--25. (New) A method for obtaining antibodies specific for human pancreatic elastase iso-enzymes comprising:

immunizing a vertebrate animal with an immunogenic composition comprising a conjugate consisting of a non-elastase carrier protein and a peptide selected from the group consisting of

NH_2-A-V-K-E-G-P-E-Q-V-I-P-I-N-COOH (SEQ ID NO: 2),

NH_2-Y-T-N-G-P-L-P-D-K-L-Q-Q-A-R-COOH (SEQ ID NO: 3),

NH_2-G-P-L-N-C-P-T-E-D-G-G-W-Q-COOH (SEQ ID NO: 4),

NH_2-R-S-G-C-N-G-D-S-G-G-P-L-N-COOH (SEQ ID NO: 5),

NH2-S-L-Q-Y-E-K-S-G-S-F-Y-COOH (SEQ ID NO: 15),

NH2-F-G-C-N-T-R-R-K-P-T-V-F-T-COOH (SEQ ID NO: 16),

NH2-G-G-E-E-A-R-P-N-S-W-P-W-Q-COOH (SEQ ID NO: 10),

NH2-S-S-S-R-T-Y-R-V-G-L-G-R-H-N-COOH (SEQ ID NO: 11),

NH2-K-D-W-N-S-N-Q-I-S-K-G-N-D-COOH (SEQ ID NO: 12),

NH2-G-P-L-N-C-Q-A-S-D-G-R-W-COOH (SEQ ID NO: 13), and

NH2-G-A-L-P-D-D-L-K-Q-G-R-L-COOH (SEQ ID NO: 14)

to induce formation of antibodies in the immunized vertebrate animal; and

separating and purifying the formed antibodies from the immunized animal to obtain polyclonal antibodies specific for human pancreatic elastase iso-enzyme; or

fusing B-cells from the immunized animal with a myeloma cell line and selecting and cloning hybridoma cell lines to obtain monoclonal antibodies specific for human pancreatic elastase iso-enzyme.

26. (New) The method of claim 25 wherein the vertebrate animal is selected from rabbits, guinea pigs, goats, chickens or fish.

27. (New) The method of claim 26 wherein the vertebrate animal is a chicken.

28. (New) The method of claim 25 wherein the non-elastase carrier protein is selected from hemocyanin or albumin.

29. (New) An isolated and purified polyclonal antibody specific for human pancreatic elastase iso-enzymes made by a method comprising:

immunizing a vertebrate animal with an immunogenic composition comprising a conjugate consisting of a non-elastase carrier protein and a peptide selected from the group consisting of

NH_2-A-V-K-E-G-P-E-Q-V-I-P-I-N-COOH (SEQ ID NO: 2),

NH_2-Y-T-N-G-P-L-P-D-K-L-Q-Q-A-R-COOH (SEQ ID NO: 3),

NH_2-G-P-L-N-C-P-T-E-D-G-G-W-Q-COOH (SEQ ID NO: 4),

NH_2-R-S-G-C-N-G-D-S-G-G-P-L-N-COOH (SEQ ID NO: 5),

NH2-S-L-Q-Y-E-K-S-G-S-F-Y-COOH (SEQ ID NO: 15),

NH2-F-G-C-N-T-R-R-K-P-T-V-F-T-COOH (SEQ ID NO: 16),

NH2-G-G-E-E-A-R-P-N-S-W-P-W-Q-COOH (SEQ ID NO: 10),

NH2-S-S-S-R-T-Y-R-V-G-L-G-R-H-N-COOH (SEQ ID NO: 11),

NH2-K-D-W-N-S-N-Q-I-S-K-G-N-D-COOH (SEQ ID NO: 12),

NH2-G-P-L-N-C-Q-A-S-D-G-R-W-COOH (SEQ ID NO: 13), and

NH2-G-A-L-P-D-D-L-K-Q-G-R-L-COOH (SEQ ID NO: 14)

to induce formation of the antibodies in the immunized vertebrate animal; and

isolating and purifying the formed antibodies from the immunized animal to obtain

the polyclonal antibodies specific for human pancreatic elastase iso-enzyme.

30. (New) A diagnostic method for determining a disorder of pancreatic function in a human patient at risk for or suspected of having a disorder of pancreatic function comprising:

providing one or more different purified polyclonal antibodies each elicited against an immunogenic composition comprising a conjugate consisting of a non-elastase carrier protein and one or more synthetic peptides selected from the group consisting of

NH_2-A-V-K-E-G-P-E-Q-V-I-P-I-N-COOH (SEQ ID NO: 2),

NH_2-Y-T-N-G-P-L-P-D-K-L-Q-Q-A-R-COOH (SEQ ID NO: 3),

NH_2-G-P-L-N-C-P-T-E-D-G-G-W-Q-COOH (SEQ ID NO: 4), and

NH_2-R-S-G-C-N-G-D-S-G-G-P-L-N-COOH (SEQ ID NO: 5),

wherein said different antibodies are each specific for human pancreatic elastase;

obtaining a sample of a bodily fluid or stool from the patient;

reacting the sample with the one or more different purified antibodies to form specific immune complexes among the antibodies and human pancreatic elastase present in the sample;

detecting an amount of the immune complexes to determine an amount of human pancreatic elastase in the sample, wherein the amount of human pancreatic elastase in the sample is indicative of pancreatic function in the patient.

31. (New) The diagnostic method of claim 30 wherein the bodily fluid sample is a sample of serum, plasma, or pancreatic juice.

32. (New) The diagnostic method of claim 30 wherein the sample is a stool sample.

33. (New) The diagnostic method of claim 30 wherein at least two different antibodies are provided and the method is a sandwich enzyme linked immunosorbent assay wherein the sample is reacted with a solid phase carrier-immobilized at least one of the antibodies and a detectably-labeled at least different one of the antibodies.

34. (New) A diagnostic kit for determining a disorder of pancreatic function or determining mucoviscidosis in a human patient comprising:

one or more different purified polyclonal antibodies each elicited against an immunogenic composition comprising a conjugate consisting of a non-elastase carrier protein and one or more synthetic peptides selected from the group consisting of

NH_2-A-V-K-E-G-P-E-Q-V-I-P-I-N-COOH (SEQ ID NO: 2),

NH_2-Y-T-N-G-P-L-P-D-K-L-Q-Q-A-R-COOH (SEQ ID NO: 3),

NH_2-G-P-L-N-C-P-T-E-D-G-G-W-Q-COOH (SEQ ID NO: 4), and

NH_2-R-S-G-C-N-G-D-S-G-G-P-L-N-COOH (SEQ ID NO: 5),

wherein said different antibodies are each specific for human pancreatic

elastase.

35. (New) The diagnostic kit of claim 30 for performing a sandwich enzyme linked immunosorbent assay wherein the kit comprises at least two different antibodies and wherein at least one of the antibodies is solid phase carrier-immobilized and at least one different of the antibodies is detectably labeled. --

Remarks

The art made of record and not relied upon is considered pertinent to applicant's disclosure.

Sziegoleit et al. (Clin. Biochem. 22: 79, 1989) teach elicitation of polyclonal antibodies to purified enzyme in several animal species, including rabbits ,and the enzyme preparation used would inherently have been a mixture of at least the elastase I isoforms (i.e. elastases IIIA and IIIB), comprising some of the peptides as instantly claimed. The reference teaches a sandwich enzyme-linked immunosorbent assay for diagnosis of pancreatitis or pancreatic cancer by determining pancreatic elastase 1 using the polyclonal antibodies.

Scheefers et al. (U.S. Pat. No. 5,622,837) teach determinations of pancreatic elastase 1 in serum and stool samples as indicative of pancreatic disease. The reference teaches determinations with sandwich immunoassays involving antibodies, preferably monoclonal, elicited to different epitopes of the protein, including the use of antibodies specific for particular epitopes therein elicited by immunization with purified

enzyme or fragments thereof, as a sensitive alternative to radioimmunoassay. The referenced also teaches elicitation of polyclonal antibodies to purified elastase.

Tani et al. (J. Biol. Chem. 263: 1231, 1988) teach the amino acid sequences encoded by human elastase genes (see Fig. 9). The reference teaches that the sequence identified therein as elastase I is not expressed in human adult pancreas (see page 1231, col. 2) and that the sequences identified therein as elastase III are human elastase I as known to the art (see page 1237, col. 2).

Harlow et al. teach that, once the amino acid and/or nucleic acid sequences of a protein are known, it is routine and conventional in the art to elicit antibodies to peptides and/or fusion proteins derived from the protein and/or to prepare a bank of site-specific monoclonal antibodies for use (pages 72-77). Harlow et al. teach rationales for the selection of synthetic peptides as immunogens and suggest the carboxyl-terminal or amino-terminal peptide sequences or internal hydrophilic regions as desirable starting peptide immunogens (page 76).

Geokas et al. (J. Biol. Chem. 252: 61, 1977) teach an immunoassay for human elastase II in human serum and the elevation of the enzyme therein in individuals with acute pancreatic inflammation (see page 66, col. 2).

Schneider et al. (Clin. Chem. 51: 1052, 2005) teach complications if antibodies in a human elastase detection assay bind to porcine elastases.

The abstract of Weiss et al. (published variously in: J. Ped. Gastroenterol. Nut.; Pancreatology; and Pancreas) teaches that antibodies produced by the instant assignee (BIOSERV) and used in assays of stool elastase do not bind to all isoforms of elastase.

Further experimentation is taught as required by the reference for one to assess the specific differences and prognostic value of elastase isoforms in the assessment of exocrine pancreatic insufficiency.

Stein et al. (Clin. Chem. 42: 222, 1996) teach the clinical evaluation of the fecal elastase assay of Scheefers et al. (US 5,622,837).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 11 a.m. to 7 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, SPE, can be contacted at (571) 272-0806.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/J. L. G./
James L. Grun, Ph.D.
Examiner, Art Unit 1641
January 30, 2012

/GAILENE R. GABEL/
Primary Examiner, Art Unit 1641
1/28/12